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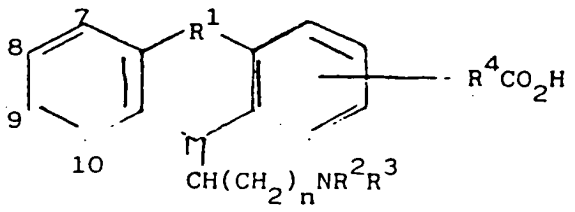
(54) Tricyclic compounds.

(57) The present invention provides a compound of formula (I)



or a salt, ester or amide thereof, wherein R^1 is $-CH_2-CH_2-CH_2-O-$ or $-O-CH_2-$. R^2 and R^3 are the same or different and are each hydrogen, C_{1-4} alkyl or taken together with the nitrogen comprise a nitrogen-containing heterocyclic ring having four to six ring members; R^4 is a single bond or a C_{1-7} bivalent aliphatic hydrocarbon group may be joined to the aromatic ring system at the 2, 3, 8 or 9 positions, n is 0 to 3, processes for its preparation and intermediates therefor, pharmaceutical compositions containing it and its use in medicine.

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This formulation is prepared in a similar way to the nasal spray.

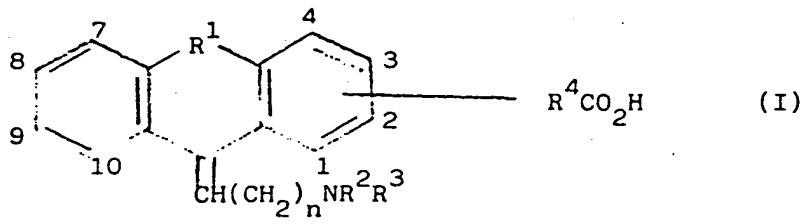
(J)-Topical Cream

Ingredient		Amount per 100.0 g
Active Compound		0.1 g
Emulsifying Wax, N.F.		15.0 g
Mineral Oil		5.0 g
White Petrolatum		5.0 g
Preservative		0.25 g
Purified Water	q.s.	100.0 g

The preservative is dissolved in approximately 50 g of warm purified water and after cooling to about 25°-30° C the compound of formula (I) is added. In a separate container the emulsifying wax, mineral oil and white petrolatum are mixed well and heated to approximately 70°-80°C. The aqueous solution containing the compound of formula (I) is added to the warm mixture of emulsifying wax, mineral oil and petrolatum with vigorous mixing while cooling to 25° C. Additional purified water is added with mixing to bring the total weight of the cream to 100.0 g.

Claims

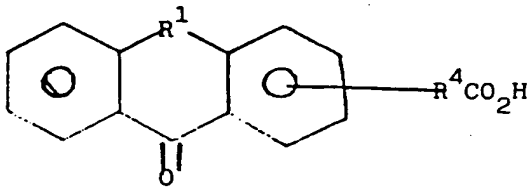
1. A process for the preparation of a compound of formula (I)



(I)

or a salt, ester or amide thereof; wherein R^1 is $-CH_2-CH_2-$, CH_2-O- or $-O-CH_2-$; R^2 and R^3 are the same or different and are each hydrogen, C_{1-4} alkyl or taken together with the nitrogen comprise a nitrogen-containing heterocyclic ring having four to six ring members; R^4 is a single bond or a C_{1-7} bivalent aliphatic hydrocarbon group and may be joined to the aromatic ring system at the 2, 3, 8 or 9 positions; n is 0 to 3 which process comprises;

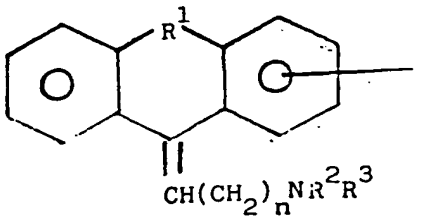
a) the reaction of a compound of the formula (III):



wherein R^1 and R^4 are as hereinbefore with an appropriate Wittig reagent or with an appropriate Grignard reagent followed by dehydration or

b) when it is required to prepare a compound of the formula (I) wherein R^4 is a single bond by the carboxylation of a compound of the formula (V) above: wherein A^1 to R^3 and n are as hereinbefore defined and X is a hydrogen or halogen atom, or

c) the hydrolysis of a compound of the formula (V):



(V)

wherein X is R^4CN:

d) wher it is required to prepare a compound of the formula (I) wherein R^4 is other than a single bond by reacting a compound of the formula (V) wherein X a halogen atom and R^1 and R^3 and n are as hereinbefore defined with a compound: $CH_2=CHR^6COR^7$ in which R^6 is a C_{1-5} bivalent aliphatic hydrocarbon and R^7 is a protecting group and thereafter removing the protecting group when required, and

e) thereafter converting one compound of the formula (I) to another compound of the formula (I) if desired

2. A process according to claim1B for the preparation of a compound of formula (II):

3. A process according to claim 1 for the preparation of a compound selected from:
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-3-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-3-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-8-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-8-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-9-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-9-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-acrylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-acrylic acid
(E)-5-(3-(Dimethylamino)propylidene)-10,11-dihydro-5H-dibenzo[a.d]cyclohepten-3-carboxylic acid
(Z)-5-(3-(Dimethylamino)propylidene)-10,11-dihydro-5H-Dibenzo[a.d]cyclohepten-3-carboxylic acid

4. A pharmaceutical composition comprising a compound of formula (I) as defined in claim 1 in admixture with a pharmaceutically acceptable carrier.

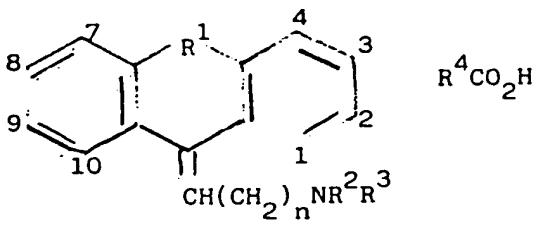
5. A process for the preparation of a pharmaceutical composition which comprises bringing a compound of the formula (I) as defined in claim 1 into association with a pharmaceutically acceptable carrier.

6. A novel chemical intermediate of the formula (III) or (IV).

7. A method for the control of allergy which comprises the administration of a compound of the formula (I) as defined in claim 1.

CLAIMS FOR AUSTRIA.

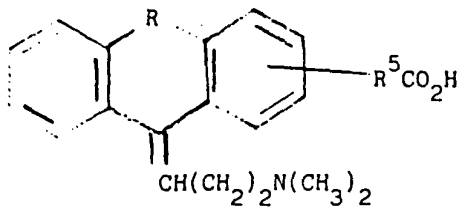
1. A compound of formula (I)



(I)

or a salt. ester or amide thereof; wherein R^1 is $-CH_2-CH_2-$, CH_2-O- or $-O-CH_2-$; R^2 and R^3 are the same or different and are each hydrogen, C_{1-4} alkyl or taken together with the nitrogen comprise a nitrogen-containing heterocyclic ring having four to six ring members; R^4 is a single bond or a C_{1-7} bivalent aliphatic hydrocarbon group and may be joined to the aromatic ring system at the 2, 3, 8 or 9 positions: n is 0 to 3.

2. A compound of formula (II)



(II)

or a salt, ester or amide thereof: wherein R_1 is $-CH_2-CH_2$, $-CH_2-O-$ or $-O-CH_2$; and R^5 is a single bond or -CH=CH joined to the aromatic ring system at the 2, 3, 8 or 9 positions.

3. A compound of claim 2 selected from:
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-3-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-3-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-8-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-8-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-9-carboxylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-9-carboxylic acid
(E)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-acrylic acid
(Z)-11-(3-(Dimethylamino)propylidene)-6,11-dihydrodibenz[b.e.]oxepin-2-acrylic acid
(E)-5-(3-(Dimethylamino)propylidene)-10,11-dihydro-5H-dibenzo[a.d]cyclohepten-3-carboxylic acid
(Z)-5-(3-(Dimethylamino)propylidene)-10,11-dihydro-5H-Dibenzo[a.d.]cyclohepten-3-carboxylic acid

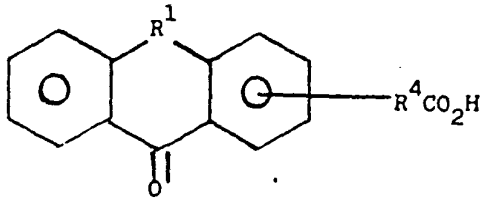
4. A pharmaceutical composition comprising a compound of formula (I) as defined in claim 1 in admixture with a pharmaceutically acceptable carrier.

5. A compound of the formula (I) as defined in claim 1 for use in medicine

6. A compound of the formula (I) as defined in claim 1 for the manufacture of a medicament for the control of allergy.

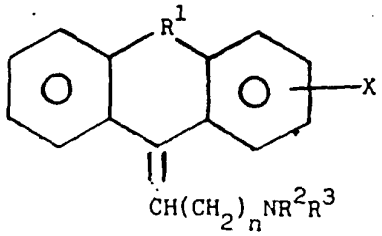
7. A compound of the formula (I) as defined in claim 1 for the manufacture of a medicament for relieving the detrimental effects of histamine, for the control or relief of the effects of an asthmatic condition, or for controlling bronchoconstriction or bronchospasm characteristic of allergic asthma.

8. A process for the preparation of a compound of formula (I) as defined in claim 1 which comprises
a) the reaction of a compound of the formula (III):



(III)

wherein R^1 and R^4 are as hereinbefore with an appropriate Wittig reagent or with an appropriate Grignard reagent followed by dehydration or
b) the hydrolysis of a compound of the formula (V):



(V)

wherein X is R^4CN;
c) when it is required to prepare a compound of the formula (I) wherein R^4 is a single bond, a

carboxylation reaction on a compound of the formula (V) above wherein A^1 to R^3 and n are as hereinbefore defined and X is a hydrogen or halogen atom, or

d) when it is required to prepare a compound of the formula (I) wherein R^4 is other than a single bond the reacting of a compound of the formula (V) above wherein X a halogen atom and R^1 to R^3 and n are as hereinbefore defined with a compound: $CH_2=CHR^6COR^7$ in which R^6 is a C_{1-5} bivalent aliphatic hydrocarbon and R^7 is a protecting group and thereafter removing the protecting group when required, and

e) thereafter converting one compound of the formula (I) to another compound of the formula (I) if desired

9. A novel chemical intermediate of the formula (III) or (V).

carboxylation reaction on a compound of the formula (V) above wherein A^1 to R^3 and $_n$ are as hereinbefore defined and X is a hydrogen or halogen atom, or

d) when it is required to prepare a compound of the formula (I) wherein R^4 is other than a single bond the reacting of a compound of the formula (V) above wherein X a halogen atom and R^1 to R^3 and n are as hereinbefore defined with a compound: $CH_2 = CHR^6COR^7$ in which R^6 is a C_{1-5} bivalent aliphatic hydrocarbon and R^7 is a protecting group and thereafter removing the protecting group when required, and

e) thereafter converting one compound of the formula (I) to another compound of the formula (I) if desired

9. A novel chemical intermediate of the formula (III) or (V).